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Assistant Commissioner for Patents  
Washington, D.C. 20231

On 10-15-01

TOWNSEND and TOWNSEND and CREW LLP

By: Linda Sheffer

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

SHAN *et al.*

Application No.: 09/848,990

Filed: May 3, 2001

For: TREATMENT OF  
HYPERTRIGLYCERIDEMIA AND  
OTHER CONDITIONS USING LXR  
MODULATORS

Examiner: Not yet assigned

Art Unit: 1645

COMMUNICATION UNDER

37 C.F.R. §§ 1.821-1.825

AND

PRELIMINARY AMENDMENT

Box SEQUENCE  
Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

In response to the request to comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures, 37 C.F.R. §§ 1.821-1.825, that accompanied the Notice to File Missing Parts of Nonprovisional Application mailed July 13, 2001, Applicants submit herewith the required paper copy and computer readable copy of the Sequence Listing. Please amend the specification as follows.

**In the Specification:**

Please replace the paragraph beginning at page 5, line 13, with the following:

--Figure 5 shows the location of putative LXR response elements in the human SREBP-1a and SREBP-1c upstream regions. Also shown is the nucleotide sequence (SEQ ID NO:1) of the region upstream of exon 1c, which region includes the promoter for human SREBP-1c. Putative LXR $\alpha$  response elements are underlined.--

Please replace the paragraph beginning at page 6, line 20, with the following:

--Figure 11. The sequence of PCR primers (SEQ ID NOS:2-21) used for amplifying mouse cDNA probes.--

Please replace the paragraph beginning at page 26, line 11, with the following:

--To form a chimeric receptor for use in the assay of the invention, the ligand binding domain and the DNA binding domain are linked together. Suitable methods of forming such linkages are known to those of skill in the art. For a review of methods for constructing fusion proteins between receptor ligand binding domains and DNA binding domains, *see, e.g., Mattioni et al., Methods in Cell Biology* 43(Pt A):335-352 (1994). The linkage can be done using either recombinant or chemical methods. For example, a cysteine residue can be placed at either end of a domain so that the domain can be linked to another domain by, for example, a sulfide linkage. More typically, the ligand binding domains and DNA binding domains are joined by linkers, which are typically polypeptide sequences, such as polyglycine sequences of between about 5 and 200 amino acids, with between about 10-100 amino acids being typical. In some embodiments, proline residues are incorporated into the linker to prevent the formation of

significant secondary structural elements by the linker. Preferred linkers are often flexible amino acid subsequences which are synthesized as part of a recombinant fusion protein. In one embodiment, the flexible linker is an amino acid subsequence comprising a proline such as Gly(x)-Pro-Gly(x) (SEQ ID NO:22) where x is a number between about 3 and about 100. A linker can also be a single peptide bond, or one or more amino acid residues. In other embodiments, a chemical linker is used to connect synthetically or recombinantly produced ligand binding domain and DNA binding domain subsequences. Such flexible linkers are known to persons of skill in the art. For example, poly(ethylene glycol) linkers are available from Shearwater Polymers, Inc. Huntsville, AL. These linkers optionally have amide linkages, sulfhydryl linkages, or heterofunctional linkages.--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 6, at the end of the application.

REMARKS

Applicants request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing the above named sequences, SEQ ID NOS:1-22, in computer readable form, and a paper copy of the sequence information which has been printed from the floppy disk.

The information contained in the computer readable disk was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy. This amendment contains no new matter.

Attached hereto is a marked-up version of the changes made to the Specification and Abstract by the current Amendment. The attached pages are captioned **"VERSION WITH MARKINGS TO SHOW CHANGES MADE."**

PATENT

Respectfully submitted,

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Specification:**

Paragraph beginning at line 13 of page 5 has been amended as follows:

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